REMARKS

The Office Action and the cited and applied reference have been carefully reviewed. No claim is allowed. Claims 93-120 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 94-120 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. This rejection is respectfully traversed.

Claim 120 is now amended, thereby obviating the rejection with regard to claim 120.

Claim 94 is held to be indefinite for omitting essential elements. Applicants believe that claims 95-97 are inadvertently included in this rejection because these claims are dependent from claim 93, not claim 94. Regarding claim 94, the hybridization conditions are of sufficiently high stringency (60°C for hybridization is high stringency) that the wash is not considered an essential element. While a wash step is preferred only to remove labeled probe that is not hybridized, the wash conditions are irrelevant because the high stringency hybridization conditions during hybridization would have already eliminated any significant non-specifically or loosely hybridized probe.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 93-96 and 98-118 have been rejected under 35 U.S.C. §112, first paragraph, as the examiner holds that enablement is not commensurate in scope with the claims for the reasons set forth in the previous Office Actions, paper nos. 22, 24, and 29. The examiner states that the claims encompass antibodies that bind to epitopes of the variants which are not found in the particularly disclosed sequence, SEQ ID NO:2. This rejection is respectfully traversed.

Claim 93 is now amended to further define the variant as that which has the same antigenic fragment(s) as in (i), i.e., IGIF or IL-18, having the physicochemical properties as recited in (1) to (4) of claim 93. Applicants believe that the recitation of "has the same antigenic fragment(s) as in (i)" is implicitly supported by the specification even though it is not literally and explicitly disclosed in the specification.

The specification as filed, from page 15, line 21, to page 16, line 21, discloses a monoclonal antibody of the present invention, i.e., a monoclonal antibody specifically recognizes IGIF (IL-18). In particular, on page 16, lines 4-5, it is disclosed that the monoclonal antibody can be obtained by using the protein or its antigenic fragments as an antigen. "The protein" means, of course, IGIF (IL-18). It is therefore taught

in the specification that a monoclonal antibody which specifically recognizes IGIF (IL-18) can be obtained by using IGIF (IL-18) or its antigenic fragments as an antigen. It is further apparent to those of skill in the art that the "antigenic fragment" used as an antigen should have the same antigenicity as IGIF (IL-18). Accordingly, those of skill in the art would clearly understand that the presently claimed monoclonal antibody should specifically recognize a variant of IGIF (IL-18) having the same antigenic fragment(s) as in IGIF (IL-18) as well as IGIF (IL-18) *per se*. Applicants submit that the recitation of "has the same antigenic fragment(s) as in (i)" in claim 93 is supported by the specification as filed.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 93-96 and 98-118 have been rejected under 35 U.S.C. §112, first paragraph, as lacking adequate written description for the variants of SEQ ID NO:2, for the reasons set forth in the previous Office Actions, paper nos. 22, 24, and 29. This rejection is respectfully traversed.

Claim 93 is now amended to recite "to be used to obtain said monoclonal antibody" after "the same antigenic fragment(s) as in (i)". Applicants believe that a monoclonal antibody that specifically recognizes a variant which has the same antigenic fragment(s) as in IGIF (IL-18) to be used to obtain said

monoclonal antibody is described in the specification as filed, in particular, from page 15, line 21, to page 16, line 21.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 93-120 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Nakamura et al., Infect. Immun. 61:64-70 (1993), for the reasons set forth in the previous Office Actions, paper nos. 22, 24, and 29. The examiner holds that the factor of Nakamura et al. is the same as the IGIF or IL-18 of the present invention. This rejection is respectfully traversed.

The Okamura et al. reference, Infect. Immun. page 3966-3972 (1995), cited by the examiner discloses on page 3966, right column, middle paragraph, lines 6-8:

> The serum factor whose apparent molecular mass was previously found to be 75 kDa by gel filtration was shown to contain the same 18- to 19-kDa IGIF. (emphasis added)

Okamura thus teaches that Nakamura's factor contains isolated 18- to 19-kDa IGIF and but never suggests that Nakamura's factor is as a whole the same substance as IGIF.

Furthermore, Okamura suggests at page 3969, left column, second paragraph, that Nakamura's factor is a substance which is formed with isolated 18 to 19 kDa IGIF and some other proteins bound to IGIF. Since such a substance is a mixture of more than one proteins, it is impossible even for a skilled

person to obtain monoclonal antibody specific to IGIF using the mixture, i.e., impure IGIF, even if the mixture contains IGIF. This is well known in the art.

In addition, although Nakamura et al. disclose that mouse serum contains a substance having IGIF activity, Nakamura et al. did not succeed in isolating pure protein having IGIF activity. It is only two years after Nakamura's publication that Okamura was able to successfully isolate the pure protein having IGIF activity. The examiner states:

> The state of the art at the time of the present invention was filed has well established that a monoclonal antibody to a specific protein is highly desirable because of its high specificity and easy production in large quantities, and a method of producing monoclonal antibodies had been well known and widely practiced. (emphasis added)

However, it should be noted that homogeneous (pure) protein had been required in order to obtain monoclonal antibodies at that time the present invention was filed even though a method of producing monoclonal antibodies had been well known and widely practiced. In other words, homogeneous IGIF or IL-18, or a variant thereof having the same antigenic fragment(s) as defined in claim 93 are indispensable in obtaining monoclonal antibodies to IGIF/IL-18. Since Nakamura discloses neither homogeneous IGIF (IL-18) as a homogeneous antigen nor a variant thereof having the same antigenic fragment(s), applicants believe that it would have been impossible even for a skilled person to obtain a monoclonal

antibody as defined in claim 93 based on the Nakamura's disclosure.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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